Akinyemi Ojesina [1,2], Gabriela Soriano [3], Bruce J. Walker [2], Robert J. Soiffer [4], Joseph H. Antin [5], Lindsey Baden [6], Jason Hornick [7], Francisco Marty [4], Matthew Meyerson [1,2]. [1] Dana-Farber Cancer Institute; [2] Broad Institute; [3] Memorial Sloan-Kettering Cancer Center; [4] Dana-Farber Cancer Institute, Boston, MA; [5] Hematologic Malignancies, Dana-Farber Cancer Institute, Boston, MA; [6] Brigham and Women's Hospital, Boston, MA; [7] Brigham and Women's Hospital

Innate and therapy-induced states of immunosuppression are associated with a variety of potentially infectious idiopathic clinical syndromes. Using unbiased, next-generation sequencing, we investigated the metagenome of cord colitis syndrome (CCS), a recently described transplantation-associated colitis syndrome, in order to identify a candidate infectious trigger. Shotgun whole genome sequencing of DNA was performed followed by computational classification of reads. A large proportion of reads remained unmapped, suggesting the presence of a potentially novel organism. In order to investigate the source of these unmapped reads, *de novo* computational assembly of nonhuman reads was performed and yielded 98 contigs of $>$ 2.5kb in length covering a total of 7.65Mb. Read coverage and GC content was similar for all of these contigs, suggesting they corresponded to a common organism. Phylogenetic analysis of this draft genome revealed that this organism was a novel species, which we have provisionally named *Bradyrhizobium enterica*. PCR confirmed the presence of B. enterica in three additional CCS patients and demonstrated absence of B. enterica in normal colon, colon cancer and graft-versus-host disease controls. In summary, we have demonstrated the assembly of a novel bacterial draft genome from human tissue specimens without isolation or culture of the organism. This organism, provisionally named B. enterica, is associated with CCS suggesting that it may function as an opportunistic human pathogen.

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An Identical Reduced Intensity Conditioning (RIC) Regimen Prior to Allogeneic (ALLO) Hematopoietic Stem Cell Transplantation (HSCT) in 222 Patients with Hematologic Malignancies: A Monocenter Experience

Didier Blaise [1], Luca Castagna [2], Geoffroy Venton [3], Roberto Crocchiolo [3], Jean EL-Cheikh [3], Sabine Furst [4], Claire Oudin [5], Angela Granata [3], Norbert Vey [6], Réda Bouabdallah [6], Christian Chabannon [7]. [1] Bone Marrow Transplant Unit, Institut Paoli Calmettes, Marseille, Cedex 9, France; [2] Unité de Greffe, Institut Paoli-Calmettes, Marseille, France; [3] Unité de Greffe, Institut Paoli-Calmettes, Marseille, France; [4] Institut Paoli Calmettes; [5] Institut Paoli-Calmettes; [6] Hematologie, Institut Paoli-Calmettes, Marseille, France; [7] Transplant and Cellular Therapy Unit, Institut Paoli Calmettes, Marseille, Cedex 9, France

Introduction: We have treated 222 consecutive patients eligible for allo HSCT with the same RIC from June 2005 up to March 2012. We particularly studied the impact of age, donor source and of the recent disease risk index (DRI) published by Amand et al (Blood 2012).

Patients and methods: All patients were treated for hematologic malignancies and were prepared with Fludarabin (30 mg/m^2/D x 5 D, IV Busulfan (3.2 mg/Kg/D x 2 D, and rabbit antithymocyte globulin (rATG) (2.5 mg/Kg/D x 2 D). All patients received CSA from D-1 with the addition of MMF in case of MMUD as post graft immunosuppression.

Table 1

*	Total
N	222
Age	58 (20-72)
HCT-SCI 0-1/2/>3	53/54/90
PS 90-100/70-80/50-60	107/108/7
AML/ALL/MDS/NHL and HD/MM/others	76/10/22/71/35/8
Disease Risk index Low/Int/High/VHigh	26/132/58/6 12%/59%/26%/3%
MRD/MUD/ MMUD	111/77/34 50%/35%/15%

* HCT-SCI indicates: hematopoietic cell transplantation specific comorbidity index; MRD, Matched related donor; MUD, Matched unrelated donor; MMUD, Mismatched unrelated donor

Table 2

	n	2-y OS	2-y PFS	2-y RR	2-y NRM
All patients	222	64%	54%	28%	20%
Low DRI	26 (12%	92%	69%	8%	13%
Int DRI	132 (59%)	69%	56%	27%	21%
High/VHigh DRI	64 (29%)	43%	40%	38%	31%
$>$ 58 years	120	61%	50%	/	27%
$<$ 58 years	102	67%	60%	/	16%
MRD	111	67%	53%	/	16%
MUD+ MMUD	111	60%	55%	/	28%

Results: As for August 2012, follow-up is 24 months (4-77). Patients characteristics are presented in Table 1; median age was 58 years with 45% and 30% of the patients presenting with a HCT-SCI $>$ 2 and a high or very high DRI respectively. 50% of donors were related siblings. Analyses of outcomes are presented in Table 2. Age only influenced NRM (P = .21). Donor origin has no influence on any outcome variable. DRI influenced OS (P = .000017) (Figure 1), PFS (P = .00045) (Figure 2), relapse (P = .0073) and at a lesser degree NRM (P = .056).

Conclusions: Overall results are promising. They validate the previously published DRI and indicate populations where efforts should be focused. Interestingly results are similar whatever the donor is.

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Post-Transplant Outcome in Patients with Acute Myeloid Leukemia and Myelodysplasic Syndrome Who Received Conditioning Regimen Based on Fludarabin, Busulfan and Anti-Thymoglobulin Prior to Allogeneic Hematopoietic Stem Cell Transplantation

Didier Blaise [1], Claire Oudin [2], Patrice Chevallier [3], Sabine Furst [4], Thierry Guillaume [5], Jean EL-Cheikh [2], Roberto Crocchiolo [2], J. Delaunay [6], Anne Etienne [7], Norbert Vey [7], Mohamad Mohty [8]. [1] Bone Marrow Transplant Unit, Institut Paoli Calmettes, Marseille, Cedex 9, France; [2] Unité de Greffe, Institut Paoli-Calmettes, Marseille, France; [3] Hematologie, CHU NANTES, Nantes, France; [4] Institut Paoli Calmettes; [5] University of Louvain, Brussels, Belgium; [6] Institut Paoli-Calmettes; [7] Hematologie, Institut Paoli-Calmettes, Marseille, France; [8] Hematology Dpt, CHU de Nantes-Hotel-Dieu, Nantes, France

Purpose: Over the years, we have tuned the chemotherapy dose intensity of a busulfan based RIC regimen with the aim to better control disease while retaining a low toxicity profile. Here, we retrospectively analyzed a cohort of patients with myeloid malignancies treated identically in two French centers.

Patients and methods: From 2005 to 2010 in Marseille and Nantes we transplanted 165 patients (median age: 56.8 years

(range:18-71); males: 83, females: 82) presenting AML (N=124) or MDS (N=41) following a similar conditioning regimen but for the dose of busulfan (Bu): 1/Fludarabine (30 mg/m^2/day over 5 days) 2/, rabbit ATG (r-ATG) (2.5mg/kg/day over 2 days) and 3/ i.v. or oral Busulfan (Bu) (130 mg/m^2/day or 3.2 mg/kg respectively over 2 to 4 days) (table 1). Cyclosporin A was given as post graft immunosuppression. Initially higher Bu doses were proposed to patients under the age of 55, without comorbidities and with higher risk diseases.

Results: With a median follow up of 20.7 months, 2 year overall survival (OS) and PFS were 59.6% (95% CI: 51.8-68.6) and 54.9% (95% CI: 47-64) respectively. Grade 2-4 and 3-4 acute graft-versus-host diseases (aGvhD) at day 100 was 19.4% and 7.9% respectively. cGvhD (all grades) and extensive cGvhD were 25% and 14.4% at 1 year post transplantation respectively. Non relapse mortality (NRM) was 11.7 and 15.4% at 12 and 24 months. Relapse (CIR) was 24% and 29.7% at 1 and 2 years.

Overall neither the patient age, nor the donor type or the dose of Busulfan influenced significantly OS, PFS or CIR in the whole cohort. Surprisingly, NRM was lower after 3 or 4 days busulfan conditioning regimen (3.6% vs 21.3%,$P = .009$).

The 93 CR1 AML patients had 2-year OS and PFS of 63.4% (95% CI: 53.3-75.3) and 60.9% (95%CI: 50.8-72.9) respectively. Two-year OS reached 66.4% (95%CI: 56.4-81.8) for AML patients with favorable or intermediate karyotype and 50.5% (95%CI: 33-77.3) for unfavorable, $P = .08$. AML patients with favorable or intermediate karyotype tend to have a better 2-year PFS (63.8%, 95%CI: 52.2-78.1) than unfavorable karyotype (52%, 95%CI: 34.5-78.3), $P = .2$.

Patients under the age of 55 (n=76) present overall a better outcome than older (OS: 63.9 (CI: 52.7-74.4) vs 56% (CI: 45.6-68.7), $P = .2$, PFS: 60.5 (49.7-73.8) vs 50.4% (CI: 40-63.5),$P = .2$, NRM: 9.4 vs 20.3%, $P = .07$). In addition higher doses of BU improved OS (77.5% vs 47.9%, $P = .058$), PFS (71.6 vs 46.4%, $P = .1$), without increase of NRM (2.2% vs 18.7%, $P = .03$).

Conclusion: This conditioning regimen using Fludarabin, Busulfan and r-ATG can result in good OS and PFS probabilities, in myeloid malignancies. Given the patient population characteristics the NRM can be considered as low. The good NRM profile of higher doses invite to further developments.

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Reduced Intensity Transplants Using G-CSF-Mobilized Hemopoietic Cells From Haploidentical Related Donors

Kenneth Bradstock [1], John Kwan [2], Kenneth Micklethwaite [3], David Gottlieb [4], Emily Blyth [2], Gillian Huang [5], Stephanie Deren [2], Mark Hertzberg [6]. [1] BMT Service, Westmead Hospital, Sydney, Australia; [2] Haematology, Westmead Hospital, Sydney, Australia; [3] Haematology, Westmead Hospital, Westmead, Australia; [4] Department of Medicine, Westmead Hospital, University of Sydney, Sydney NSW, Australia; [5] Haematology Clincal Trials Office, Westmead Hospital, Westmead, NSW, Australia; [6] Department of Haematology, Westmead Hospital, Westmead, Australia

Aim: To determine the safety and feasibility of using G-CSF-mobilized peripheral blood progenitor cells from haploidentical related donors for transplantation in patients with poor-risk hematological malignancies receiving reduced intensity conditioning therapy and post-transplant cyclophosphamide as GVHD prophylaxis.

Methods: Nine patients aged 33 to 65 years (median 48) with poor prognosis hematological malignancies (4 AML, 1 MDS, 2 Ph+ ALL, 1 DLBCL, 1 ALL) who lacked HLA-matched related or unrelated donors underwent transplantation using G-CSF-mobilized PBSC from haploidentical relatives, after receiving reduced intensity conditioning therapy with fludarabine, cyclophosphamide, and single fraction TBI 200 cGy. GVHD prophylaxis consisted of cyclophosphamide 50 mg/kg IV daily on days +3 and +4, followed by daily oral tacrolimus and mycophenolate. Median follow-up is 11 months (1-14). Results were compared with a previous cohort of 12 patients receiving unmanipulated haploidentical bone marrow.

Results: Neutrophil and platelet recovery (ANC >1.0 median day 18, range 11-35 ; platelets >20 median day 19, 1-45) was comparable with 15 and 17 days respectively,for bone marrow. Six patients had neutropenic fevers, but there was no mucositis, use of TPN, or early transplant-related death. Six of 8 assessable patients had complete donor chimerism in blood T cells and granulocytes at day +28. Two had graft rejection with only host DNA (one patient with MDS with high-titre anti-donor HLA antibodies, and one patient with ALL), as compared with 2 rejections of 12 previous patients receiving bone marrow grafts. Of the 6 patients with complete donor chimerism, 1 had stage 3 skin acute GVHD, but there has been no chronic GVHD or disease relapse. The MDS patient with graft rejection was re-transplanted after plasmapheresis and rituximab and IV cyclophosphamide/busulphan conditioning with PBSC from an alternative haploidentical related donor, and identical GVHD prophylaxis, and achieved complete donor chimerism.

Conclusion: The use of unmanipulated G-CSF-mobilized HPC collected from haploidentical relatives appears feasible for patients receiving reduced intensity conditioning and high-dose cyclophosphamide as GVHD prophylaxis, with rates of engraftment, graft rejection and GHVD comparable to that seen with haploidentical bone marrow. This protocol offers an allogeneic transplant option with low cost and toxicity for patients without a HLA-identical donor.

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Evaluation of Transjugular Liver Biopsy in the Diagnosis of Early Hepatic Dysfunction After Allogeneic Hematopoietic Cell Transplantation

Nerea Castillo [1,2], Pere Barba [3], Mercedes Perez [4], Helena Allende [5], M Aranzazu Gelabert [5], Francesc Bosch [5], David Valcarcel [2,3]. [1] Hematology, Hospital Vall d'Hebron, Universitat Autònoma de Barcelona, Barcelona; [2] Hospital Vall d'Hebron. Universitat Autònoma de Barcelona, Spain; [3] Hematology, Hospital Vall d'Hebron. Universitat Autònoma de Barcelona; [4] Interventional radiology, Hospital Vall d'Hebron. Universitat Autònoma de Barcelona; [5] Hospital Vall d'Hebron. Universitat Autònoma de Barcelona

Introduction: Liver biopsy might be necessary in the diagnosis of liver dysfunction after allogeneic stem cell transplantation (allo-SCT) but transparietal (TP) access is usually not possible. Transjugular liver biopsies (TJLB) may offer a good alternative. We retrospectively analyzed the role of TJLB in the diagnosis of early hepatic dysfunction after allo-SCT.

Methods: We included all consecutive allo-SCT recipients undergoing TJLB in our centre from May 1997 to September 2011. Median follow-up for survivors was 28 months (1-57). According to our protocol, TJLB instead of TP access was preferred in patients with platelet count <50x10e9/L, coagulation abnormalities or unstable medical condition. TJLB were performed using a needle coated with a flexible catheter through jugular access. Pathological samples were analyzed by an experienced pathologist in the centre and retrospectively revised.